REMARKS

Claims 44-52 are active in the case.

35 U.S.C. 112, 1st paragraph and claim objection 37 C.F.R. 1.75(c)

Dependent claims 49 and 50 are rejected on grounds that recited terms such as "containing sweetener" and "solubilizing agent" are broader than the corresponding base claim, which uses the transitional phrase "consisting essentially of" with regard to the chemical composition. However, the mere addition of a sweetener or a solubilizing agent would not change the essential nature of the invention, so the base claim does encompass such additives. The Examiner appears to be interpreting the phrase "consisting essentially of" as fully closed language, just like the phrase "consisting of," which is not correct.

Rejections over Prior Art

The present invention relates to an osteoporosis treatment using effervescent bisphosphonate compositions having a selected pH of 4.5 to about 5.5, and very high buffering capacity, causing the stomach to rapidly eject the effervescent solution. The claims closely track the compositions of Examples 3, 4 and 5, with the lower limit of the buffering system quantity at 4.3 grams vs. 3.36 grams.

The applicants have recognized that a buffered, low pH environment inhibits acid rebound (the natural process of acid secretion that occurs whenever food enters the stomach), and that a large quantity of the buffer system (4.3 grams or more total weight) causes the stomach to eject the effervescent solution quickly. This combination reduces the esophageal irritation often seen with bisphosphonates. (Hayward Declaration ¶7)

Claims 44-52 are rejected under 35 USC 103(a) as being obvious over Katdare et al. (US 5,853,759).

Katdare et al. teaches generically that bisphosphonates can be administered in effervescent solution. but did not recognize that it isn't enough to merely dissolve the bisphosphonate in an effervescent system, or that a relatively large amount of buffering reagents promotes rapid ejection of the effervescent solution from the stomach, and so helps prevent gastric irritation. The Examiner asserts that Katdare et al. have provided a similar solution to the same problem, i.e., gastric irritation. However, the present invention is directed to compositions

having a large amount of the buffering system (4.3 to about 6 grams total weight, with a relatively high minimum percentage of acid), at a specific pH range of 4.5 to about 5.5. This combination of pH and buffering capacity is not disclosed by Katdare et al., nor are the benefits of it suggested by the reference. The Rohrich Declaration shows that the Katdare et al. examples typically have a pH of 6.1 or more, which would be expected to promote *acid secretion* by the stomach due to the acid rebound effect, and would not be as effective for administering bisphosphonates. (Hayward Declaration ¶9)

The pH of Katdare et al.'s Example 1 is lower at 4.3, but its acid neutralizing capacity (ANC) is also very low, only 2.95 mEq of acid per dose. That is because it contains very little of the acid and alkaline components; just enough to dissolve the solids, but not enough to provide significant acid neutralizing capacity. The Katdare et al. formulas all have very low total weights of about 1.1 - 2.5 grams, compared to 4.35 - 6 grams in the present invention. The small quantities of the effervescing system in Katdare et al. would not promote rapid ejection of the bubbling solution from the stomach, and so would be prone to cause more irritation for that reason as well. (Hayward Declaration ¶11). This is not the same solution to the problem provided by Katdare et al.

Claims 44 - 52 are rejected under 35 U.S.C. 103(a) as being obvious over Daifotis et al. (US 5,994,329).

Example 8 of Daifotis et al. is a liquid bisphosphonate composition of pH 6.75 (column 19, lines 40-62), which is *not effervescent*. Clearly it is not the same solution to the problem provided by this invention. The Daifotis et al composition contains 1,500 mg trisodium citrate dihydrate and 56.3 mg citric acid, but no effervescencing alkaline component. The ANC per dose is only 6.9 mEq (see the Table of the Rohrich Declaration) due to the small quantity of buffering components. Without any carbonate or bicarbonate the solution generates no bubbles and so would not be ejected from the stomach as rapidly as the highly effervescent solutions of the present invention. Accordingly, the rejection for anticipation under 35 U.S.C. 102(b) should be withdrawn.

CONCLUSION

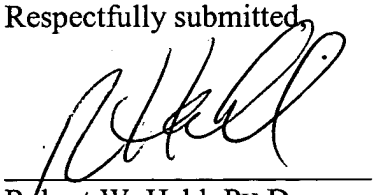
Applicants submit respectfully that the present application is in condition for allowance.

Undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 625-3680. All correspondence should be directed to our Chicago address given below.

AUTHORIZATION

Applicants believe all fees due in connection with this filing are being paid herewith. However, the Commissioner is hereby authorized to charge any fees due in connection with this filing to Deposit Account 50-1710 or credit any overpayment to same.

Respectfully submitted,



Robert W. Hahl, PH.D.
Registration No. 33,893

Dated:: **December 29, 2005**

Patent Administrator
KATTEN MUCHIN ROSENMAN LLP
525 West Monroe Street
Chicago, Illinois 60661-3693
Facsimile: (312) 902-1061